SUPPLEMENTAL REMARKS

The Examiner failed to find support in the specification for a method of reducing inflammation comprising administering botulinum toxins B-G. In the amendment filed on November 5, 2001, applicant stated in response to this rejection:

> In the seventh paragraph of the "Background of the Invention", applicant discloses that "botulinum is known to exist as immunotypes A-G", and that "each immunotype has been associated with varying durations of action and chemodenervating potency per LD 50 unit, as described by Borodic, G.E., Pearce, L.B., New Concepts in Botulinum toxin Therapy, Drug Safety 11(3): 145-152, 1994." The cited article describes the particular relative potencies per LD 50 unit of various immunotypes A-G of botulinum toxin. Thus, one of ordinary skill in the art could easily, and without undue experimentation, determine the appropriate dose of any of immunotypes B-G based upon the effective doses of immunotype A disclosed in the working examples of the specification. The potency relative to immunotype A could easily be determined by one of skill in the art simply by looking at the reference cited above, which was published well before the filing date of the present application. For example, the cited article clearly discloses that immunotype B exhibits a relative potency per LD 50 unit that is 1/50 to 1/100 that of immunotype A. Thus, one of ordinary skill in the art, without any undue experimentation , would be able to treat inflammation using a dose of botulinum toxin B in LD 50 units that is 50 to 100 times the dose disclosed in the specification as effective for botulinum toxin A. Furthermore, physicians skilled in the art titrate the dose upward from lower levels as individual variation in botulinum toxin dose response does occurs from patient to patient. This titration is not undue experimentation—rather, it is within the scope of ordinary medical practice in the use of pharmaceutical agents to treat human patients.

Applicant would like to clarify and expand upon those remarks by noting several other references that also indicate that dose selection for treating inflammation with other subtypes of botulinum toxin would be understood by

one of skill in the art in light of the disclosure in the specification of appropriate doses of botulinum toxin type A. Borodic GE et al. Botulinum B toxin as an alternative to botulinum A toxin : a histologic study. Ophthalmic Plastic and Reconstructive Surgery 9(3), 182-90, 1993. Tsui JK, Hayward M, Mak EK, Schulzer M Botulinum toxin type B in the treatment of cervical dystonia Neurology 45 (11), 2109-10, 1995. Lew MF et al. Botulinum toxin type B: A double-blind, placebo-controlled, safety and efficacy study in cervical dystonia. Neurology 49, 701-06, 1997. Applicant has enclosed copies of these three references herewith.

Applicant also notes that dose standardization of botulinum toxin preparations, whether of the same or of different subtypes, may be achieved through routine procedures described in U.S. Patent Nos. 5,183,462; 5,298,019; and 5,401,243, enclosed herewith. Applying any of these procedures to determine the dose of a subtype other than type A that is equivalent to the dose of type A that is disclosed in the specification of the instant application would be routine, and would not constitute undue experimentation.

In addition, applicant would like to note that the particular dose ranges of botulinum B toxin disclosed in the references cited above, and cited in the amendment filed on November 5, 2001, should not be considered as limiting the scope of the claimed invention. These references indicate that physicians skilled in the art may titrate the dose of botulinum toxin through well-

understood procedures, as individual variation in botulinum toxin dose response occurs from patient to patient. This titration is not undue experimentation—rather, it is within the scope of ordinary medical practice in the use of pharmaceutical agents to treat human patients.

In light of the foregoing and the amendment filed on November 5, 2001, applicant submits that pending claims 2, 3, and 4 in this application are in condition for allowance, and a favorable action by the Examiner with respect to those claims is respectfully requested. Applicant further submits that claims 1, 5-8, 10-12, and 17-23 are in condition for allowance in every respect except with regard to the rejections over U.S. Patent No. 6,063,768. As explained in the amendment filed November 5, 2001, applicant has filed a Request to Declare Interference between the present application and the '768 patent.

If the Examiner is of the opinion that it would assist in placing claims 2, 3, and 4 in condition for allowance, and claims 1, 5-8, 10-12, and 17-23 in condition for allowance other than with regard to the prior art rejections over the '768 patent, or otherwise expedite prosecution, the applicant invites the Examiner to contact his counsel by telephone at the number listed below.

No additional extension of time is believed necessary for this filing. However, to the extent that any extension of time or other fee is deemed necessary for this filing, the Commissioner is hereby authorized to charge such

extension of time or other fees which may be required for this paper to Deposit Account Number 13-3250, Order No. 33677-00000.

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service, with sufficient postage, as Express Mail (Label No. EL708704438US) in an envelope addressed to: Asst. Commissioner for Patents, Box Amendments, U.S. Patent and Trademark Office, Arlington, VA 22202 on January 7, 2002:

Maria Lagdameo
Signature

Maria Lagdameo

Respectfully submitted,

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